American Journal of Pharmacy

AND THE SCIENCES
SUPPORTING PUBLIC HEALTH

DEAN EDWARD SPEASE
Recipient of the 1952 H. A. K. Whitney Lecture Award
by the Michigan Society of Hospital Pharmacists

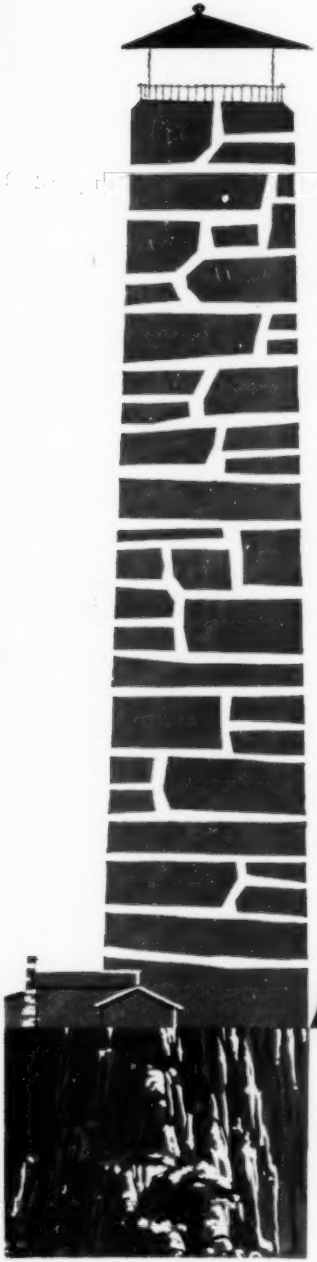
Since 1825 *February 1952*

American Journal of Pharmacy

Published monthly by the Philadelphia College of Pharmacy and Science
43d Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription, $4.00 — Foreign Postage, 25 Cents Extra
Single Numbers, 40 Cents — Back Numbers, 50 Cents

Entered as Second-Class Matter March 27, 1937, at the Post Office at Philadelphia, Pa.
Under Act of March 3, 1879



constant vigilance

Quality must be without qualification. It is a thing to be proved, not claimed. Even the maker himself is not sure of the quality of his product unless his operations include the accepted practices of standardization and control. Even then, constant vigilance must be exercised if quality is to be insured.

Quality has always been the major factor in the Lilly Laboratories. Lilly Products are made first, then priced—not made to fit a price previously established. Quality is a scientific fact, not just a word, a theory, or a selling argument. Only in this manner can the Red Lilly be accepted as the flower of pharmaceutical aristocracy.

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U.S.A.

clear the way!

To clear congested nasal passages such as develop in colds and sinusitis . . . to promote aeration and free drainage . . NEO-SYNEPHRINE® is the preferred vasoconstrictor decongestant of a tremendous number of physicians.

Make sure you are adequately stocked with the various forms of NEO-SYNEPHRINE which will be in demand during winter months as a result of Winthrop-Stearns detailing and medical advertising.

NEO-SYNEPHRINE Hydrochloride

¼% solution, plain or aromatic. 1 oz., 4 oz. and 16 oz. bottles
½% solution, 1 oz. bottles
1% solution, 1 oz., 4 oz. and 16 oz. bottles
½% water soluble jelly, ⅝ oz. tubes

NEO-SYNEPHRINE THENFADIL®

Nasal solution, 1 oz. bottles
Nasal jelly, ⅝ oz. tubes

NEO-SYNEPHRINE with PENICILLIN

¼% Neo-Synephrine, 10,000 units Penicillin per cc., bottles of 15 cc

NEO-SYNEPHRINE SULFATHIAZOLATE

0.6% solution, 1 oz. and 16 oz. bottles

Neo-Synephrine and Thenfadil, Trademarks reg. U. S. & Canada

Winthrop Stearns INC., 1450 BROADWAY, NEW YORK 18, N. Y.

in demand the year around

CHLOR-*TRIMETON*
maleate

It pays to keep up your stock of Chlor-*Trimeton*® Maleate (chlorprophenpyridamine maleate) throughout the year because it is as effective in nonseasonal allergies as it is in hay fever. The volume of Chlor-*Trimeton* Maleate prescriptions indicates the faith physicians have in this potent, well tolerated antihistamine that gives prompt, prolonged relief.

CHLOR-*TRIMETON*
maleate

is available in *four* forms:

Chlor-*Trimeton* Maleate Tablets—4 mg., for rapid action when only a few doses daily are required, or when symptoms are intermittent.

Chlor-*Trimeton* Maleate Repeat Action Tablets—8 mg., for both rapid and prolonged action. Suggested for alleviation of chronic, recurrent allergic symptoms. One tablet gives 8 to 10 symptom-free hours.

Chlor-*Trimeton* Maleate Syrup—2 mg. per 4 cc., for children and adults who prefer a liquid medication. Pleasantly flavored and compatible with many drugs.

Chlor-*Trimeton* Maleate Injection—2 mg. per cc., for rapid control of severe allergic disorders by intramuscular, intravenous, or subcutaneous route.

CHLOR-*TRIMETON*

Schering CORPORATION · BLOOMFIELD, NEW JERSEY

when they want

penicillin or penicillin with dihydrostreptomycin

physicians will now ask for

S-R* or S-R-D*

(Parke-Davis procaine penicillin and buffered crystalline penicillin for aqueous injection)

(Parke-Davis penicillin and dihydrostreptomycin)

Physicians will ask for S-R because they know this well established combination of soluble and repository penicillin provides the early, high and prolonged blood levels they need for maximum therapeutic efficacy. And when they want a broader bacterial spectrum, they'll order S-R-D (penicillin and dihydrostreptomycin). Intensive, sustained promotion is helping to make S-R and S-R-D important business in pharmacies throughout the country.

Packaging *S-R:* Supplied in rubber-diaphragm-capped vials containing 400,000 units, 2,000,000 units, and 4,000,000 units each. Dilution as directed yields a 1-cc. single-dose; a 5-cc. five-dose; or a 10-cc. ten-dose suspension, each cubic centimeter of which contains 300,000 units of crystalline procaine penicillin-G and 100,000 units of buffered crystalline sodium penicillin-G. S-R is supplied in individual cartons and packages of ten vials.

S-R-D, 1 Gm.: Each vial contains 300,000 units of procaine penicillin-G, 100,000 units of buffered crystalline sodium penicillin-G, and dihydrostreptomycin sulfate equivalent to 1 Gm. of dihydrostreptomycin base. When 2.2 cc. of diluent is added, this provides sufficient material to permit withdrawal of 2 cc. from the vial for a single dose injection.

S-R-D, ½ Gm.: Each vial contains 300,000 units of procaine penicillin-G, 100,000 units of buffered crystalline sodium penicillin-G, and sufficient crystalline dihydrostreptomycin sulfate to represent ½ Gm. of dihydrostreptomycin base. When 1.5 cc. of diluent is added, this produces 2 cc. of material for injection.

*Trademark

PARKE, DAVIS & COMPANY

MEDICAMENTA VERA · PD CO.

AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

Vol. 124 FEBRUARY 1952 No. 2

CONTENTS

OUR COVER

DEAN Edward Spease, formerly dean of the School of Pharmacy at Western Reserve University in Cleveland, has been named to receive the 1952 H. A. K. Whitney Lecture Award by the Michigan Society of Hospital Pharmacists. The award, established in honor of the first chairman of the American Society of Hospital Pharmacists, is presented annually to a person who has made outstanding contributions to hospital pharmacy.

The selection of Dean Spease was made in recognition of his many contributions to hospital pharmacy, which included the development of the first Minimum Standard for Pharmacies in Hospitals. This development was accepted in 1936 by the American College of Surgeons at a meeting in San Francisco. The first graduate course in hospital pharmacy was organized and directed by Dean Spease beginning in 1937. His educational interest in hospital pharmacy was further exhibited by his offering instruction in hospital pharmacy to all undergraduate pharmacy students at Western Reserve at the time. Dean Spease's many articles which appeared in hospital publications during the 1930's reflect the work of a hospital pharmacy pioneer who recognized the need for the pharmacist to become an active member of the professional team in hospitals. He advocated the establishment of hospital pharmacy internships, the use of a formulary in hospitals and the establishment of a pharmacy and therapeutics committee. Dean Spease has been previously distinguished for his work in hospital pharmacy with an honorary Master of Science degree from the Philadelphia College of Pharmacy and Science in 1936.

Dean Spease served nine years as a faculty member of the College of Pharmacy at Ohio State University and was dean at Western Reserve from 1916 to 1940. During the last eight years of his deanship he was directing pharmacist of the University Hospitals in Cleveland. From 1940 to 1944 he was the Director of Public Relations for the National Association of Retail Druggists and since 1948 has been Science and Prescription Editor of the *N. A. R. D. Journal.*

E D I T O R I A L

THE D-H AMENDMENT—AN INDICTMENT OF PHARMACY

SO much has been spoken and written concerning the merits and demerits of the Durham-Humphrey Amendment that one almost need apologize for presuming to add anything of consequence to the discussion. As one reads the various viewpoints expressed it is difficult, if one is purely objective, not to form the opinion that most of those participating are motivated by self-interest regardless of what aspect of the question is being presented.

At the very outset it should have been evident to all honest pharmacists that no prescription should be refilled unless it were almost certain that the physician would endorse such action. Yet pharmacists, by and large, refilled prescriptions *ad libitum* with little or no regard for the patient's welfare or the physician's wishes. Quite some time ago we commented editorially on this sad state of affairs but to no avail.

Pharmacists, for too long, have considered the economic aspects of the refill business as of far more importance than the violation of professional ethics which such unrestrained practice entailed. Had this not been the case the Food and Drug Administration would not have been led into reading into the Food and Drug Act of 1936 a ban on refills which actually did not exist.

It was the assumed economic threat involved, we fear, which led the National Association of Retail Druggists to champion the *original* Durham-Humphrey Bill, and it is certain that its proponents never expected to get what is now enacted into law. When it became evident that a law of some sort was to be enacted all interested parties became involved in an effort to get its provisions as reasonable as possible.

The American Pharmaceutical Association in the beginning refused to concede that the Food and Drug Act gave legal backing to the ban on refills and in this it was right. The Association, however, was not sufficiently forthright in facing the evil which the F. D. A. sought to correct.

As matters now stand the F. D. A. has a law, making it possible for them to *force* pharmacists to do what they should have done all along. This becomes the pattern of our civilization. As we fail to live up to our responsibilities as citizens new laws are passed supposedly to correct the attendant evils created. But as less and less is left to individual initiative and decision our moral fiber is weakened and we lose the ability to act with vision, responsibility, and courage.

It is this trend in all civilized countries—wherein self-interest is the prime motivating force, expediency the rule of the day, and compromise with evil the sign of wisdom and statesmanship—which will eventually lead to regimentation and autocracy, such as the world has never seen. Only a world-wide acceptance of the philosophy expressed by the phrase, "I am my brother's keeper" with all that this entails can stem the tide of gross materialism and human debasement. The professions dedicating themselves to the relief of human suffering should be the foremost among those wherein such a philosophy is practiced. The Durham-Humphrey Amendment serves not only as a legal whip coercing pharmacists into more proper conduct; it is also a lasting reminder of our professional failure.

L. F. Tice

ERRATA

Vol. 123, p. 335:

Penicillin O should have its chemical name given as allyl mercaptomethylpenicillin.

Vol. 123, p. 345:

The chemical name for Bentyl Hydrochloride should be: β-diethyl-aminoethyl-1-cyclohexy-cyclohexanecarboxylate hydrochloride.

CLARIFICATION OF GLYCYRRHIZA FLUIDEXTRACT U. S. P.

By Nathan A. Hall *

THE manufacture of Glycyrrhiza Fluidextract U. S. P. is complicated by clarification difficulties. These problems are greater with some lots of drug than with others. Generally however, filtration is a problem due to the complex colloid system created.

In the official process (1), the drug is percolated with boiling water; the percolate is treated with diluted ammonia solution and boiled under atmospheric pressure to remove the excess ammonia and water. At this point the procedure calls for filtration from which arises the major difficulty. At times the percolate is almost unfilterable or so difficult to filter that loss of extractive results. Since no control standard for the finished product exists, there may be considerable variation between finished fluidextracts. This study was undertaken to improve the filtration step.

Experimental

Enzyme Clarification

Common natural plant colloids are starch, hemicelluloses, pectic substances, and proteins. Most of the proteins in the percolate are denatured by heat and precipitated so that they exert little colloidal activity. Of the remaining colloids, starch and pectic substances may be converted to soluble products by commercial enzyme preparations. The use of pectic enzymes is an accepted practice in the wine and apple juice industries (2, 3, 4). Therefore, a series of experiments were conducted on the percolate after concentration to determine the effect of various enzymes. The enzymes were added in a 1:1000 concentration to 100 ml. portions of the percolate and incubated for twenty-four hours at 37.5°C. The pH of the medium was 6.3. Filtration rate was measured by adding exactly 25 ml. of the cloudy supernatant liquid to a dry number 40 Whatman filter paper in a normal funnel. The filtrate was collected in a 10 ml. graduated cylinder and the volume recorded at the end of thirty minutes. Results obtained are shown in Table I.

* Research Chemist, College of Pharmacy, University of Washington, Seattle, Washington.

TABLE I

EFFECT OF ENZYMES ON GLYCYRRHIZA PERCOLATE

	Apparent ** Viscosity Before Incubation Centipoises	Apparent Viscosity After Incubation Centipoises	Volume filtered in 30 min. ml.
Control	10	10	3.6
Taka-diastase	10	7	7.4
Amylopsin	10	8	5.6
Pancreatin	10	8	5.7
Trypsin	10	8	5.2
Papain	10	10	2.2
* Pectinol M	10	8	7.2
Pectinol M-Taka-diastase	10	7	7.4

* Supplied by Rohm and Haas Company, Philadelphia, Pa.
** By Berkfield Viscosimeter @ 25°C.

Taka-diastase and Pectinol M improved the filtration markedly, however when they were combined, no improvement over either enzyme used singly was noted. Pancreatic enzymes, either proteolytic or amylolytic, produced only a slight improvement in filtration. Papain impeded rather than facilitated the filtration, which might have been due to the unsatisfactory enzyme preparation.

Another series of experiments were run in which filtration was performed by means of Ertel Pressure Filter with a number 2 filter pad (coarse). Pressure was regulated at 5 to 10 p. s. i., and the average filtration rate was measured for the first ten minutes. Results were as follows:

Untreated Control—1.2 ml. per minute
Taka-diastase Treated—2.5 ml. per minute
Pectinol-M and Taka-diastase Treated—2.2 ml. per minute

The filtration was completed with the addition of filter-aid (Hyflo-Super Cel or Celite manufactured by the Johns-Manville Co.), and the fluidextracts were prepared. No difference in appearance or taste was noted between the enzyme treated fluidextract and the control.

Clarification by Sedimentation

In several industries such as the sugar (5) and wine (6) industries where filtration problems involving plant extractives have oc-

curred, the process of sedimentation has been used to rid the extract of insoluble components held in suspension by the colloid system encountered.

The agents used were selected on the basis of their possible interference with the colloid system. Two authors (7, 8) have reported the use of calcium and magnesium salts to precipitate the impurities in aqueous glycyrrhiza extracts, therefore these salts were used in the hope that the precipitation caused by them might result in a sympathetic flocculation. Casein and tannin were selected because of their use in the wine industry, and bentonite was chosen because of its use in both the sugar and wine industries.

Bentonite was introduced in the form of the U. S. P. magma (5%), and all other agents were introduced as 2% solutions. The sedimenting agent in the concentrations listed in Table II, was added to 15 ml. of the concentrated percolate in a centrifuge tube; the tubes were shaken and allowed to stand overnight (16 hours). Results were those shown in Table II.

TABLE II

EFFECT OF VARIOUS AGENTS ON THE SEDIMENTATION OF GLYCYRRHIZA PERCOLATE

Agent	Concentration	Appearance of Supernatant Liquid	Volume of Sediment (ml.)
Casein	1:500	Cloudy	1.2
	1:1000	Cloudy	1.2
	1:1500	Cloudy	1.2
Calcium Chloride	1:500	Cloudy	2.5
	1:1000	Cloudy	1.8
	1:1500	Cloudy	1.5
Magnesium Chloride	1:500	Cloudy	1.2
	1:1000	Cloudy	1.2
	1:1500	Cloudy	1.2
Bentonite	1:500	Clear	5.4
	1:1000	Clear	4.5
	1:1500	Clear	3.2
Tannic Acid	1:500	Cloudy	2.9
	1:1000	Cloudy	2.6
	1:1500	Cloudy	2.4
Control		Cloudy	1.2
Control		Cloudy	1.2
Control		Cloudy	1.1

Casein and magnesium chloride in the concentration used were without effect on the sedimentation rate; tannic acid was partially

effective but produced a bitter taste; calcium chloride was partially effective; however, bentonite was highly effective in all concentrations.

On the basis of the above experiments, several trial lots of Glycyrrhiza Fluidextract were prepared with different lots of drug. Each lot was divided into two portions; one was treated with bentonite, and one was untreated for use as a control. Empirically, a 1:1500 concentration was selected because higher concentrations exhibited undesirable suspending properties which decreased the amount of clear supernatant liquid recovered. The supernatant liquid in each case was easily filterable with a pressure filter through a coarse filter without the use of filter aid. However, for polishing filtration through a fine filter, the addition of small amounts of filter aid was necessary to remove the last traces of the bentonite which passed through the coarser filter. It was found advantageous, also, to centrifuge the sludge from the bentonite sedimentation to increase the quantity of clear percolate recovered. When the viscosity of the concentrated percolate was high, (above 20 centipoise at 25°C) bentonite sedimentation was carried out when the evaporated percolate was concentrated to twice the volume recommended by the U. S. P. After sedimentation evaporation was continued to the recommended volume before filtration.

Organoleptic evaluation on the basis of the highest dilution which was perceptible to taste showed practically no difference between fluidextracts prepared by filtration with filter-aid and filtration after bentonite sedimentation. Viscosity similarly showed no change. The average pH as measured with a Beckman Model H pH meter was slightly lower in fluidextracts prepared by bentonite sedimentation (6.2) than in those prepared without bentonite sedimentation (6.5). Comparison of the bottled samples after one month storage in bottles revealed no sediment in fluidextracts clarified with bentonite and definite sediment in the controls. On the basis of this observation, bentonite clarification also apparently improved the stability of the fluidextract.

Summary

A series of experiments were run in an attempt to improve the filtration step in the preparation of Glycyrrhiza Fluidextract U. S. P. Amylolytic and pectinolytic enzymes added in 1:1000 concentration

improved the filtration rate by partial destruction of the colloid system, however, filtration remained difficult. Sedimentation with bentonite 1:1500 resulted in a clear percolate, easily filterable without the use of filter-aid. Comparison of finished fluidextracts made with and without the use of clarifying agents revealed no marked difference in appearance or taste when clarifying agents were used. Bentonite clarification also seemed to improve the stability of the finished fluidextract.

BIBLIOGRAPHY

(1) "United States Pharmacopeia," Fourteenth Revision, Mack Publishing Co., Easton, Pa., 1950, p. 267.

(2) Cruess, W. V. and Kilbuck, J., *Wines and Vines, 28,* 23 (1949).

(3) Yang, H. Y., Thomas, G. E. and Wiegand, E. H., *Wines and Vines, 31,* 77 (1950).

(4) Kertesz, Z. I., "Apples and Apple Products," Interscience Publ., 1950.

(5) McCleery, W. L., *Reports Ann. Meeting Hawaiian Sugar Planters Assoc. 61,* 114 (1942).

(6) Herstein, K. M. and Jacobs, M. B., "Chemistry and Technology of Wines and Liquors," Second Edition, D. Van Nostrand Company, Inc., 1948, p. 205.

(7) K. K. Kanegahuchi Boseki, Japanese Patent 109, 401, Jan. 29, 1935; German Patent 662, 834, July 22, 1938 through *Chem. Abstracts 32,* 9405.

(8) Ito, Y. British Patent 457,349, Nov. 26, 1936.

STUDIES ON THE ROOTSTOCKS OF NUTGRASS I.

By John Y. P. Wu † and Henry M. Burlage ††

Introduction

CYPERUS rotundus L. (Nutgrass)* of the Sedge family is one of nineteen species that have been reported indigenous to South Central Texas. It is an extremely troublesome weed which is a "perennial by long scaly tuber-bearing rootstocks, culms 1 to 6 dm. high, sharply triangular, strongly striate, often from corm-like bases, not tufted. The leaves are flat, shorter than the culm, 2 to 6 mm. wide, septate-nodulate below, those of the involucre 3 to 5, the longer exceeding the inflorescence. The umbel is simple or compound, 3 to 10 rayed, the primary rays as much as 8 cm. long, usually with reddish sheath-like bases; the spikelets are numerous, 5 to 25 mm. long, 2 mm. wide, acute, loosely clustered reddish-brown or purple-brown, commonly with two hyaline, green-centered empty scales at base. Scales are closely appressed, 3.0 to 3.5 mm. long, 2 mm. wide; stamens 3 mm. style about the length of the achene; stigmas 3 exserted; achenes linear-oblong to obovoid, 3 angled, 1.0 to 1.5 cm. long" (1).

The species described on the preceding page is an extremely annoying weed in the gardens and fields of South Central Texas and it was observed that the ground rootstocks possess a pepper-like odor indicating the presence of a volatile oil, which might impart properties to the ground rootstocks, with a possibility of their use as a condiment, even as a substitute for pepper.

Experimental

The dried tuber-bearing rootstocks were ground to a No. 50 powder in a hammer mill and were extracted by percolation in two ways: (a) by means of selective solvents in the following order—petroleum ether, ether, choloform, absolute alcohol, 70% alcohol, and water in an apparatus designed to maintain the loss of the solvent to a minimum and (b) by means of Cellosolve as recommended by Curts and Harris (2).

(†) Research Scientist, College of Pharmacy, University of Texas, Austin 12, Texas.

(††) Dean, College of Pharmacy, University of Texas, Austin 12, Texas.

(*) Our appreciation is extended to Dr. D. V. Brown of the Botany Department of the University of Texas, who verified our identification of the plant.

The results obtained by the former procedure are shown in Table I.

TABLE I

EXTRACTS OBTAINED FROM *Cyperus rotundus L.* (Nutgrass)

Solvent used	% Extract	Appearance and character of the extract	Odor
1 Petroleum Ether	2.53	Brown, thick, oily	pepper-like odor
2 Ether	1.00	Brown, fatty, waxy	sweet aromatic
3 Chloroform	0.20	Brown, waxy	milder than #2.
4 Absolute Alcohol	1.15	Dark brown, waxy	same as in #2.
5 Alcohol 70%	1.00	Resinous, firm	slight pungent
6 Water	18.34	Dark brown, gummy	not characteristic

The various extracts obtained by the Curts and Harris procedure are given in Table II.

TABLE II

EXTRACTS OBTAINED FROM *Cyperus rotundus, L.* (Nutgrass) by the Curts-Harris procedure using Cellosolve

Solvent used	% Extract	Appearance and character of the extract	Odor
1 Petroleum Ether	2.50	Oily, Dark brown, thick,	Pepperlike
2 Ether	2.25	Light brown, oily	Sweet, aromatic
3 Chloroform	0.45	Yellow, oily	Sweet, aromatic
4 Chloroform (alkaline)	trace	Yellow-waxy residue	Sweet, aromatic
5 Alcohol 95%	0.75	Dark brown, resinous	Slight pepperlike
6 Residue from H_2O Cellosolve Mixture	8.70	Black, amorphous residue	Not characteristic

Physical and Chemical Constants of the Various Extracts

These constants were determined by the usual methods and are reported for those extracts, which are in sufficient quantities. The residues were also tested qualitatively for nitrogen and sulfur by the usual tests. The results of these determinations are shown in Table III.

TABLE III.

PHYSICAL & CHEMICAL CONSTANTS OF THE VARIOUS EXTRACTS OF *Cyperus Rotundus, L.*

	Petroleum Ether Extract		Ether Extract		Chloroform Extr.		Absolute Alcohol	95% Alcohol	70% Alcohol	Water	Residue
	from Table I	from Table II	Table I	Table II	Table I	Table II	Table I	Table II	Table I	Table I	Table II
Specific Gravity	1.040	1.045	Too thick	1.020	Insufficient	Insufficient					
Congealing Point	22° C.	20°-22° C.	21°-24° C.	15°-16° C.	—	—	INSUFFICIENT				
Melting Point	—	—	—	—	65°-68° C.	14°-15° C.	AMOUNTS				
Refractive Index $(N)_d^{25}$	1.5076	1.5074	1.5177	1.4500	Too dark	1.4191	FOR				
Iodine Value	57.3-59.6	55.8-59.6	51.8-52.6	18.9-21.6	52.2-54.5	4.7-4.2 C.	THESE				
Saponification Value	235.7	153.4	124.6	120.1			DETERMINATIONS				
Nitrogen	—	—	—	—	—	—	+	+	+	+	+
Sulfur	—	—	—	—	—	—	—	—	—	+	—

+ = Present

— = Absent

Feeding Experiments

Since the rootstocks of Cyperus possess a distinctive pepper-like odor which is accentuated when in a ground condition, feeding experiments were conducted with male and female rats in order to ascertain any nutritional defects and toxicity of the product when mixed with a balanced ratio in varying amounts in case it was used as a condiment.

Six male and six female rats were used with one of each sex as controls employing a feed which has the following guaranteed analysis:

Crude protein	not	less	than	24.0%
Crude fat	"	"	"	5.0
Crude fibre	"	"	"	5.0
Nitrogen-free Extract			"	46.0

The first series lasted for thirty-three days with a feed varying from 0% to 25% by weight of ground Cyperus mixed in the above feed. In the case of the females, the control showed a gain in weight of 7.15% and test females showed an average gain of 6.04%; the control male showed a gain in weight of 46.80% and the test males an average gain in weight of 41.74%.

The second series lasted for twenty-eight days with a feed varying from 30% to 50% by weight of ground Cyperus. There was an average loss in weight in the case of the female mice of 4.64%, as compared to a loss of 1.67% in the case of the control. With the male mice, there was an average gain in weight of 2.24% as compared to an 8.44% gain in weight in the case of the control. The male on the 50% by weight feed showed a loss in weight of 4.17%.

One of the females gave birth to a litter of nine on the eleventh day of the first series; the young were weaned on the third day of the second series and were maintained on a 15% by weight of nutgrass diet for forty-four days showing an average gain of 2.3 gm./a day and were in good general appearance at the conclusion of the experiment.

It would appear that both females and males tolerated well a diet up to 25% by weight of nutgrass although in both cases the gain in weight was not as great as in the controls. Diets of 30% by weight of nutgrass and above were not tolerated well since all of the females lost weight and the males showed an average gain of about one-fourth of that of the control over the same period of time.

It was observed that in the case of feeds with the higher percentages of nutgrass the animals tended to scratch the feed out of the feeders; no doubt, in an effort to find particles which were not nutgrass.

Summary

1. The rootstocks and tubers of *Cyperus rotundus L.* (nutgrass) were subjected to extraction by selective solvents and by the Curts-Harris procedure using Cellosolve as the primary solvent.

2. The various extracts are described as to appearance and odor and, where feasible, the physical and chemical constants are reported.

3. Feeding experiments indicated that white rats tolerated reasonably well diets up to and including 25% by weight of ground nutgrass rootstocks and tubers in a commercial feed. With diets containing 30% to 50% of the ground material the test animals did not thrive as well as those fed a diet with lower proportions. In fact, all female animals lost weight.

4. The loss or lowered gain in weight was probably not due to any harmful organic action but due to a lack of desire for the mixed diets since all of the animals showed gains comparing well with the controls when the normal diet was reinstated.

5. Further studies on the aromatic principles are contemplated.

REFERENCES

(1) Reeves, R. G. and D. C. Bain. "Flora of South Central Texas." The Exchange Store, A & M College of Texas, College Station, Texas. 1947, page 38.

(2) Curts, George D. and Lloyd E. Harris, *J. Am. Pharm. Association, 38*, 468, (*1949*).

HISTORICAL ASPECTS OF MUMMY IN PHARMACY AND MEDICINE

By Simon Mendelsohn *

THE precise date of the origin of Egyptian mummification by artificial means is not known although there is some presumptive evidence to indicate the practice may probably have been inaugurated at a period closely following the Second Dynasty (ca. 3400-2980 B. C.). Induced or artificial mummification referred to above, is in contrast to bodies that had been merely dessicated spontaneously by exposure to the sun or burial in hot sands over long periods. Incidentally, an extremely dry environment is the essential feature common to both of these cases. The earliest known actual Egyptian mummy is supposedly the one discovered in 1892 by Prof. Flinders Petrie near the Pyramid of Medum; this specimen was at first assumed to have been contemporaneous with the Pyramid Age (ca. 2900-2625 B. C.) until Reisner and others, in studies of subsequent data, concluded the era of the Fifth Dynasty (ca. 2750-2625 B. C.) as being the most probable.

Pliny, (23-79 A. D.) the renowned writer of classical antiquity, recommended the use of bitumen or mummy substance for medicinal purposes on the basis of traditional precept, advocating its use for

> ". . . curing of boils, coughs, asthma, epilepsy, . . . inflammation of the eyes, and blindness. . . ."

That writer was also cognizant of the probability of the drug referred to as "mumia" as having been scraped from mummies which had been removed from Egyptian tombs.

Most of the Arabic physicians of antiquity, notably Avicenna (980-1037 A. D.) held natural bitumen in the highest esteem for a wide range of therapeutic applications. Avicenna regarded the drug as being "subtle and resolutive" and by this token, useful in cases of abcesses and eruptions, fractures, concussions, paralysis, hemicrania, epilepsy, vertigo, spitting of blood from the lungs, affections

* Cincinnati, Ohio.

of the throat, coughs, palpitation of the heart, debility of the stomach, nausea, disorders of the liver and spleen, internal ulcers, and of some degree of efficacy in cases of poisoning." Powdered bitumen or finely comminuted mummy was to be administered in the form of decoctions of marjoram, thyme, elder, barley, roses, lentils, cumin seed, caraway, saffron, cassia, or parsley, along with oxymel (honey and vinegar), wines, milk, butter, castor, syrup of mulberries and other vehicles. The use of the natural bitumen as a therapeutic agent continued in vogue until the thirteenth century when the drug markets of Alexandria commenced the extensive distribution of anciently mummified flesh as a substitute. This was due either to scarcity of supplies, exorbitant prices, trade duplicity, or innovational demands suggested by a rising tide of empiricism. All of these factors may have been responsible for the natural bitumen being finally discarded in favor of powdered or fragmentary masses of Egyptian mummy that had originally been impregnated with bitumen to insure their preservation through the ages.

About the year 1200 A. D., an Alexandrian physician, one El Magar, became widely known as an assiduous prescriber of actual Egyptian mummy for both Mohammedans and Christians then in the East contending for the possession of Palestine. Henceforth, the precedent of using mummy being initiated, the physicians of all nations began to prescribe this drug for all cases of bruises, wounds, and a miscellaneous assortment of diseases in general.

Thus since the advent of the drug in the thirteenth century, Egyptian mummy came to be accepted as one of the necessary and staple commodities to be found in the apothecary shops of Western Europe and the Orient and its price increased with the ever-widening scope of its suppositious merits. This occasioned the participation of many speculators in the lucrative traffic so that more and more tombs were surreptitiously searched and as many mummies as could be found were reduced to fragments for the purpose of sale. The demands for mummy drug constantly exceeded the supply which became limited after a while, on account of restrictions imposed by the Egyptian government against the removal of the bodies from their sepulchral repositories. A combination of these circumstances contributed to inveterate temptation toward the commission of fraud, and as a result, every type of sophistication was devised and perpetrated in daily practice.

MUMMY OF SETY I OF DYNASTY XIX
COURTESY OF THE CAIRO MUSEUM

Abd-al-Latif (1161-1231 A. D.), a famous Arab medical practitioner and writer contributed enormously to the prevalent idea that miraculous cures might be effected by the use of fragments of such anciently embalmed human flesh that had been preserved in bitumens. He it was who had visited Egypt at the behest of Saladin and so to avail himself of the opportunity of studying ancient skeletons which

convinced him of the gross errors of traditional Galenic ostelogy. Abd-al-Latif also related his inquiries regarding the use of mummy, through having acquired several ancient skulls that had been removed from mummies. The skull cavities had originally been filled with from one to two pounds of bituminous matter, highly prized as a medicament among the natives on account of its unusual source.

Paracelsus (1493-1541) was also convinced of the efficacy of Egyptian mummy for the treatment of disease and considered the drug as a valuable ingredient in his famed "Sympathetic Ointment". This fantastic preparation was recommended for healing wounds by remote control; the ointment was to be applied to the instrument that inflicted a wound rather than upon the person who had sustained injury. The formula devised by Paracelsus, for the composition of this nostrum is of sufficient interest to merit its inclusion here, even though powdered mummy was but one of its several constituents.

> "Take of Boar's or Bear's fat, boil slowly for a half hour then pour on cold water. Skim off the floating fat, rejecting that which sinks. (The older the animals yielding the fat, the better). To this fat is now added, burnt worms, dried boar's brains, red sandalwood, *mummy in powder*, bloodstone, moss from the skull of a man who had died a violent death (and preferably who had been hanged) and had not been buried. The moss should be collected at the rising of the moon and under Venus, if possible, but certainly not under Mars or Saturn. With all these ingredients make an ointment and preserve in a glass vessel. This ointment must be prepared in the autumn and is of no value if an artery is severed or if the heart, brain, or liver, had suffered injury. . . ."

Once the vogue for mummy drug had begun, the demands from the physicians and apothecaries of France alone exceeded all others. Its use became quickly widespread throughout the realm, and Belon asserted that Francis I, the French king, having acquired a habit in common with others, always carried a small packet of mummy mixed with pulverized rhubarb. This was to be taken upon receiving any injury from falls or other accidents so that one thus fortified with the fanciful nostrum would presume an immunity against all common dangers.

THE SOUL VISITING THE MUMMY OF THE DEAD

In 1564, Guy de la Fontane, physician to the King of Navarre, visited Egypt to investigate the source, use, and supply, of mummy. He subsequently testified that some of the embalmed bodies alleged to have been "genuine" mummies were in reality the remains of recent slaves, criminals, lepers, vagrants, and derelicts, which had been extemporaneously treated with hot bitumen.

These bodies had been dried in the sun for some time and then bandaged; the exposure to solar heat and atmospheric dryness were prolonged until the cadaver had supposedly acquired the appearance of true Egyptian mummy. Owing to the exorbitant demand for the drug, these spurious preparations continued until the practice was exposed and consequently condemned. Fontane communicated the results of his inquiries along this line, to his good friend Paré, who in turn, made known these particulars to the public through the medium of his published works.

Ambrose Paré (1510-1590), the famed military surgeon with the French armies in 1537 and later, was suspicious of mummy as a drug and wrote of it as the "remedy" upon which most dependence

was placed in his time. He stated, however, that while this drug was so extensively prescribed, neither the physicians, the authors who had written of it, nor the apothecaries who sold it, knew anything of certainty respecting it. After enumerating the opinions of Dioscorides, Avicenna, Mathiolus, Thevet and others, and emphasizing the conspicuous diversity of their conjectures relative to "mummie," Paré condemned its usage in the following terms.

> "This wicked drugge, doth nothing helpe the diseased, in that case, wherefore and wherein it is administered, as I have tried an hundred times, and as Thevet witnesses, he tryed in himselfe when as he tooke some there of by the advice of certain physicians of Egypt, from whence it is brought; but it also inferres many troublesome symptomes, as the paine of the heart or stomacke, vomiting, and stinke of the mouth . . .
>
> "I, persuaded by these reasons, do not onely myselfe not prescribe any here of to my patients, but also in consultations, endeavor what I may, that it bee not prescribed by others. . ."

Paré also mentioned his suspicions in common with other of his time, to the effect that much of the mummy available for medicinal use in Europe had actually been prepared in France to be substituted for the genuine Egyptian article. He further alleged these sophistications to have been prepared from corpses stolen at night from the gibbets, the brain and entrails removed, and the bodies then dried in a furnace and finally immersed in molten pitch to simulate the ancient product.

Fielding H. Garrison describes Paré as a garrulous, gossipy, sometimes obscure writer who, like his medical contemporaries was addicted to the vanity of self-praise, a human trait that accompanies both great and small reputations, and was not restricted to those writers of the sixteenth century.

Olaus Wormius (1588-1654) wrote of powdered mummy as being beneficial in "contusions, clodded blood, hard labor, etc.," but his London contemporary, the sagacious Dr. Nehemiah Grewe (1641-1712) (who was probably the first to observe the existence of sex in plants, and introduced Epsom Salts to the medical profession) was quite skeptical of the efficacy of mummy when he summarized his criticisms in the following words:

> "Let them see to it, that dare trust to the old gums, which have long since lost their virtue."

Sir Thomas Browne (1605-1682) the English physician and classicist, the sage of old Norwich, resented the human greed that motivated the desecration of tombs for the purpose of obtaining a drug of questionable value, and in 1658, expressed his opinions in this direction in a beautifully written tract entitled *Urn Burial*.

> "Egyptian ingenuity . . . continuing their bodies in sweet consistencies, to attend the return of their souls. But all was vanity, feeding the wind, and folly. The Egyptian mummies which Cambyses or time hath spared, avarice now consumeth. Mummy is become mere merchandise, Mizraim cures wounds, and Pharaoh is sold for Balsams. . . ."

Bechler in 1663, included mummy among numerous other drugs equally ridiculous, and in this manner afforded some insight into the materia medica of those times.

> "Powdered human bone in red wine will cure dysentery. The marrow and oil distilled from bones is good for rheumatism. Prepared human skull is a sure cure for falling sickness, and moss grown on a skull is a hemostatic. *Mummy* dissolves coagulated blood, relieves cough, and pain in the spleen, and is very beneficial in flatulency and delayed menstruation."

The distinguished English chemist, Robert Boyle (1627-1691), was a staunch advocate of the use of mummy and described it as

> ". . . one of the useful medicines commended and given by our physicians for falls and bruises, and in other cases too. . . ."

Lord Bacon (1561-1626) of England was another famous personage who lauded the supposed merits of the drug in effect that

> "Mummy hath great force in staunching of blood which, as it may be ascribed to the mixture of balmes that are glutinous so it may also partake of a secret propriety, in that the blood draweth man's flesh."

Pierre Pomet one of the Royal Apothecaries at the Court of Louis XV of France, wrote to the effect that there were five types of mummy

then available and in use in his time. These were enumerated as follows:

(1) The Egyptian type of preparation but containing no pitch.

(2) Those in which bituminous substances had been used for embalming.

(3) From Arabian sources and preserved with myrrh, aloes, and other aromatic gums and resins; also referred to as "white mummies."

(4) Bodies dessicated in the sun in the land of the Hammonians, between Cyrene and Alexandria, these specimens being mostly the bodies of travelers buried in the quicksands.

(5) Other forms of artificially or naturally dessicated human flesh.

Pomet, resenting the fact that he was unable to stop the widespread abuses by dealers in "mummie" i. e., the nefarious practice of substitution in lieu of the Egyptian article, contented himself with admonishing purchasers of the commodity to choose only such materials as might be of a fine, shining black appearance, good odor, free from bone and dirt, and "which being burnt, does not stink of pitch" . . . and only such preparation "is proper for contusions and to hinder blood from coagulating in the body. . . ."

Nicholas Lemery, the European physician and chemist, about the end of the seventeenth century, reported that bodies which had been dessicated in the sands of Libya were in as popular demand as Egyptian mummy. By this time, mummy had become established as a drug throughout Europe and we find it sedulously recommended by physicians as being effective in healing broken and lacerated veins, and its piquancy occasioning emesis, was considered a valuable trait for the "throwing off from the stomach, collections of coagulated blood. . . ." Lemery also described mummy as being detersive, vulnerary, and resolutive, capable of "resisting gangrene"; good also for contusions, and preventing the blood from coagulating in the body. That writer was also aware of deceptions practiced with this article during his time and gave directions for the choice of highest quality "veritable mumie d'Egypte." The chief pharmaceutical preparations of mummy officially or quasi-officially recognized in some of the

European pharmacopeias and dispensatories at this time, were a Tincture, a Treacle, an Elixir, and a Balsam, the latter being described as possessed of

> ". . . piercing quality that it pierceth all parts, restores wasted limbs . . . and cures all ulcers and corruptions. . . ."

It is also interesting to note that mummy was sometimes administered as a powder in the form of a bolus in two-dram doses for the treatment of epilepsy, vertigo, palsy or to be applied to wounds to prevent gangrene, and as late as 1685, mummy was quoted in a London price list of medicinals at 5 s. 4 d. per pound. Despite the many criticisms directed against the medicinal use of this drug, and by the same token, those who prescribed it, such was the unprecedented popularity that counterfeiters of an alleged article, prepared from European cadavers reaped a prodigious harvest for quite some time.

Oswald Croll (or Crollius), a physician to Rudolph II, a seventeenth century Emperor of Germany, entertained no objections to the use of artificial mummy, and in his book, "*Royal Chymist*" proceeded to give a method for its extemporaneous preparation.

> ". . . the carcass of a young man (some said a red-haired young man) who had been killed rather than to have succumbed to disease, and it is to be presumed, had not been buried, was to lie in cold water in the air for twenty-four hours. The flesh to be cut in pieces and sprinkled with myrrh and a little aloes. This was then to be soaked in spirits of wine and turpentine for twenty-four hours, hung up for twelve hours, again soaked in the spirit mixture for twenty-four hours and finally hung up in a dry place. . . ."

That writer also recommended any type of mummy as being of great efficacy in the treatment of consumption, wasting of flesh, ulcers, and various eruptions. Crollius served the Emperor who is to be remembered as the arch-patron of the alchemists of that era, and as a member of the Rudophine Medical Academy, his efforts as well as those of his confreres, were devoted to a quest for potable gold, the philosophers' stone, and the elixir of life. In 1608 Crollius brought forth his book entitled "*Basilica chymica*" in which many new medicinal preparations were introduced to the medical profession.

Nicholas le Fevre, the French apothecary and distiller to Louis XV was invited to England by Charles II to assume charge of the laboratory of the Royal Society which, while chartered in 1662, had been founded as early as 1645. In his book, "*Compleat Body of Chymistry*" (1670), le Fevre asserted the best mummies for medical usage to be those resulting from bodies being dried in the hot sands of Libya where sometimes entire caravans were overwhelmed by simooms, and suffocated.

> "This sudden suffocation doth concentrate the spirits in all parts by reason of the fear and sudden surprisal which seizes on the travelers."

One writer in this connection, related that the bodies of young girls meeting death under these circumstances were considered far more medicinally efficaceous than others and, therefore, justified much higher price. Next to these Libyan mummies, le Fevre recommended a preparation of mummy from the dried corpse of a young man, preferably lusty, (!) from fifteen to thirty years of age, who had been suffocated or hanged. Directions were given for drying the flesh and exposing it to smoke throughout a "philosophical" month; the dried flesh was then to be reduced to fragments, powdered, mixed with old treacle (theriac) and vipers' flesh, made into an electuary with spirit of wine and so administered in one to three grain doses. This particular preparation so compounded was especially lauded as being singularly efficaceous against pestilential diseases!

As late as the eighteenth century, mummy drug was discussed by one Ephraim Chambers, who stated that this drug while not appearing to have been very ancient, did not on the other hand, become permanent in medicine. The alleged efficacy of mummy was assumed on the premise that "flesh thus embalmed was good for the cure of diverse diseases and particularly bruises to prevent the blood's gathering and coagulating. . . ." In a reference from the middle of the nineteenth century, it is apparent that the Arabs still made use of mummy powder for a medicine by mixing it with butter. This medicament, designated as "mantey" was (and probably is) esteemed as a sovereign remedy for bruises "internal and external" . . .

This then, is a more or less comprehensive narrative of the famous (or infamous) remedy that was the wonder drug of its time. The veneration of what appears to have been so useless a drug as

mummy in therapy, is typical of dogmatic empircism and superstition, a veritable collusion of fallacies that so frequently misguided the trends of medicine in the past.

By no exertion of imagination can we of this scientific age of medicine, attribute any therapeutic value to mummy substance. The fantastic nature of the drug might have served its purpose admirably, solely in the capacity of provoking psychological response in the patient. However, a more dangerous aspect was, of course, eventually encountered where the drug was ill-advisedly used to counteract serious illness. Thus diseases might grow more acute, contagion remain unchecked, and life itself be imperiled while the deluded physician and patient alike were awaiting results from a suppositious remedy that was so pitifully devoid of any intrinsic or rational value.

BIBLIOGRAPHY

Abd el Latif, *Relation de l'Egypte*, transl. by de Sacy, Paris (1810) Historias Aegypti Compend. 10th ed. translated by White, Oxford (1810).

Bacon, Francis Lord, *Sylva Sylvarum*, cant. x sec. 98.

Belon, quoted by Pettigrew, J., q. v.

Boyle, Sir Robert, *Collected Letters*, vol. 2, p. 451.

Budge, E. A. Wallace, *The Mummy*, Cambridge (1925).

Chambers, E., *Cyclopedia*, London (1738).

Danby, A., *Natural Rock Asphalts & Bitumens*, N.Y. (1913).

Dawson, W. R., *Pharmaceutical Journal 120*:518 (1928).

Dioscorides, *De Re Materia Medica*, bk. 1 chap. 100.

Garrison, F. H., *History of Medicine*, Phil. (1929).

Herodotus, *Euterpe*, (bk. 2).

Mendelsohn, S., *Embalming Fluids, N. Y.* (1940) pt. 1 (Historical) *Ciba Symposia*, May 1944 pt. 3; *The Chemist*, (N. Y.) August 1945 pp. 465-481.

Pare, Ambrose, *Collected Works*, London (1634).

Pettigrew, J., *History of Egyptian Mummies*, London (1834).

Pliny, (the Elder), *Natura Historia* vol. 2 English trans. by Holland, London (1634).

Smith, G. E. & Dawson, W. R., *Egyptian Mummies*, N. Y. (1924).

Thompson, C. J. S., *The Mystery & Art of the Apothecary*, Phil. (1929).

Wootton, A. C., *Chronicles of Pharmacy*, London (1910).

THE FIRST INTERNATIONAL PHARMACOPOEIA *

By C. H. Hampshire **

THE publication of an international pharmacopoeia is a definite contribution to the fulfillment of the first objective of the World Health Organization—the attainment by all peoples of the highest possible level of health. This book, which is the result of work begun in 1937 by a technical commission of the Health Organization of the League of Nations, represents an endeavour to further the unification of the pharmacopoeias of the world. In May 1945, during the lull in its work caused by the second World War, the commission issued an interim report in which the following reasons for unifying pharmacopoeias are set out:

> "There is a desire for a uniform system of nomenclature, and it is especially urged that the same name should, in all countries, designate a drug of the same strength and composition. Differences in national standards for widely used materials constitute a source of danger to travellers who may need to have the same prescription dispensed in different countries, not only because of the possible supply of a drug differing in strength from that to which the patient is accustomed, but also because of delays in receiving medicines that may have to be specially made or procured. Such differences, by causing confusion and misunderstanding, are also a hindrance to the spread of medical and pharmaceutical knowledge. A state of affairs under which the same supply of a drug or chemical may be accepted in one country and rejected in another may lead to the retention of lower standards in manufacture whilst the maintenance of a common high standard would tend to economy of production and would facilitate commerce between the nations" (1).

The modern developments of travel by air and the general increase in rapidity of transport strengthen the cogency of these reasons.

Brief History

Projects for the preparation of an international pharmacopoeia were mooted from time to time in the latter half of the 19th century,

* Reprinted from the *Chronicle of the World Health Organization 5*, 255 (1951).

** Formerly Secretary of the British Pharmacopoeia Commission General Medical Council Office, London.

and some unsuccessful attempts were made. Later efforts to bring about international uniformity were more restricted, attention being concentrated on the more potent drugs. Following the Brussels Conference of 1902, the first International Agreement for the Unification of the Formulae of Potent Drugs was produced and signed in 1906. The strengths of preparations and methods of procedure specified in this document were adopted in many pharmacopoeias. The second international conference was held in 1925 and the second International Agreement, which resulted from its deliberations, was completed in 1929.

The work which has resulted in the production of the *Pharmacopoea Internationalis* arose from this Agreement, which has considerably influenced the various national pharmacopoeias. The main provisions of the second Agreement deal with the unification of methods of preparation and strengths of drugs, of nomenclature, and of maximal doses. There are also the important provisions that an international organization for the unification of pharmacopoeias should be set up and that the League of Nations should be asked to constitute a permanent secretariat.

The primary purpose of the League of Nations commission was to revise and extend this International Agreement, and an early decision was that this could best be done by presenting the decisions as to formulae and strengths of drugs, names, and doses, in the form of a book—to be called the "International Pharmacopoeia"—produced on the lines of the most recent national pharmacopoeias, with complete monographs on the drugs, specifying standards, tests, and assays, and general notices, appendices on reagents, standard methods, special tests and assays, etc.

Contribution of WHO

After the war, in 1947, the Interim Commission of the World Health Organization took over the work on pharmacopoeias previously undertaken by the Health Organization of the League of Nations and set up an Expert Committee on the Unification of Pharmacopoeias to continue the work of the League's technical commission, with the following terms of reference: "to produce a draft International Agreement for the Unification of Pharmacopoeias, modifying and extending the existing Agreement for the Unification of the Formulae of Potent Drugs, and to present the draft Agreement as an

International Pharmacopoeia, similar in form to the present-day national pharmacopoeias" (2).

Since then the membership of the committee has been increased, the Permanent International Pharmacopoeia Secretariat has been established, and every encouragement and help has been given towards the production of the book which is now ready in its English and French editions. A Spanish edition is in preparation.

The first step in preparing the *Pharmacopoea Internationalis* was, of course, the selection of the drugs to be described. In making the selection, all the recent national pharmacopoeias as well as a number of official lists current in various countries were examined; valuable assistance was given by the International Pharmaceutical Federation. At a later stage the committee was helped by suggestions from the WHO expert committees which deal with such subjects as biological standardization, malaria, tuberculosis, venereal diseases, and drugs liable to produce addiction.

Description of the Pharmacopoea Internationalis

Drugs of long-established therapeutic interest which are common to a number of national pharmacopoeias are included in the *Pharmacopoea Internationalis* (Ph.I.), but the scope is not restricted to these; some drugs of recent introduction which appear likely to be generally accepted for later pharmacopoeias are also described. Neither is the scope of the Ph.I. confined to therapeutic agents; some substances used for diagnostic purposes and certain materials required for pharmaceutical purposes are likewise included.

The book comprises 199 monographs containing descriptions, standards, test, and assays designed to provide as complete a control specification as possible for each drug. There are 43 appendices defining general tests and methods and giving other data which are necessary for the understanding and use of the monographs. The methods described in the appendices have been made as complete and definite as possible so as to offer precise guidance to underdeveloped countries.

The monographs form a representative selection of the most valuable members of the various pharmacological groups—anaesthetics, analgesics, antimalarials, hypnotics, etc. Besides the vegetable, inorganic, and organic substances which are decribed in most phar-

macopoeias, sera, vitamins, hormones, and a selection from the range of sulfonamides and barbiturates are included.

The vegetable drugs of the *Pharmacopoea Internationalis* are restricted to those which have definite therapeutic activity and can be assayed chemically or biologically, e.g., opium, digitalis, ergot, belladonna, etc. An attempt has been made to give complete scientific descriptions, with details of chemical tests and assays.

Galenical pharmacy, in which those responsible for the Agreement of 1929 showed much interest, has little place in the *Pharmacopoea Internationalis.*

In completing the monographs, the various tests and assays have, as far as possible, been carried out practically on samples of the drugs actually on the market, so that the *Pharmacopoea Internationalis* is not merely a compilation made at the desk and in the committee room, but is an authoritative work containing standards and methods which have been confirmed at the laboratory bench.

In accordance with the international character of the book, the recommendations and rulings of responsible international bodies have been followed, for example, in the botanical names of drugs, in chemical names and formulae, in the atomic weights used, and in certain methods of analysis. The international biologically standardized preparations and units are those worked out by the Expert Committee on Biological Standardization and officially adopted by the World Health Organization. Review by that committee of the monographs and appendices relating to substances which are tested and standardized by biological methods has contributed considerably to the completeness of these sections of the book.

The international names of drugs are in Latin, the traditional language of medicine and pharmacy. Although the use of Latin names is being abandoned by certain national commissions, that language still remains the best medium for international purposes despite difficulties which arise in finding suitable latinized names for certain new products.

Very few synonyms are given in the *Pharmacopoea Internationalis* because of limitations of space, but a comprehensive list of alternative names has been prepared for publication.

The desire for uniformity in maximal doses expressed in the Agreement of 1929 has been extended in the *Pharmacopoea Internationalis* to include usual doses. A table gives the recommended

usual and maximal doses for adults of all the drugs described in the book; figures for single and daily doses are stated according to the mode of administration. An introductory statement indicates the procedure to be adopted when a physician desires to prescribe a larger dose than the stated maximum. Much care has been given to the compilation of this table. Leading physicians in Europe and America have been consulted through the members of the committee, and the World Medical Association has contributed useful comments.

Use of the Pharmacopoea Internationalis

The *Pharmacopoea Internationalis* has been prepared in the hope that its nomenclature, descriptions, and standards will be adopted by the national pharmacopoeia commissions. Its acceptance by those countries which already have a complete and up-to-date pharmacopoeia would do much to unify drug standards throughout the world. It is obvious that the *Pharmacopoea Internationalis* cannot be in legal conflict with national pharmacopoeias, since in any country it can have only the authority which the government of that country decides to give to it. The Third World Health Assembly has formally recommended the acceptance of the book by its Member States (3).

The *Pharmacopoea Internationalis* should be especially useful to countries which have yet to develop a national pharmacopoeia or in which the national pharmacopoeia is in need of revision in order to bring it up to date. It is hoped that the national health and pharmacopoeial authorities of such countries will decide to adopt the Ph.I. as a whole, and in its present state, as their official pharmacopoeia. In such cases, arrangements could be made for any of the editions to be supplied, in large quantities, at special low rates.

It should be mentioned that all countries are at liberty to make use of the material in the *Pharmacopoea Internationalis*, when compiling their national pharmacopoeias, without consulting the World Health Organization, but that any country wishing to publish a translation of the book in its national language under the title *Pharmacopoea Internationalis* must obtain WHO's consent and approval of the translation.

REFERENCES

(1) *Bull. Hlth Org. L.o.N.* 1945, *12*, 112.
(2) *Off. Rec. World Hlth Org.* *8*, 54.
(3) Resolution WHA3.10, *Off. Rec. World Hlth Org.* *28*, 19.

SELECTED ABSTRACTS

A Preliminary Report of Experience With the Anticoagulant, Paritol-C. Manchester, B., Hill, E. H., Rabkin, B., and Sagemen, C. B. Eastern Sect. Meet., Am. Fed. Clin. Res., Dec. 1950, through *Am. J. Med. 11*:520 (1951). An anticoagulant, Paritol-C (a polysulfated ester of dihydromannuronic acid), obtained from kelp seaweed, has shown an action similar to heparin. It was administered to 37 patients for 24 to 72 hours, and in one patient, for 7 days. The drug was administered intravenously at intervals of 8 to 12 hours in a dosage of 5 mg. per Kg. of body weight. Dicumarol was also administered simultaneously in the usual doses. The clotting time was determined prior to the administration of the drug and at intervals of 30 minutes, 1, 2, 4, 6, and 8 hours after the injection. When the clotting time was 2 to 3 times the control value of 18 to 30 minutes it was considered that effective anticoagulation had been attained.

The injection of Paritol-C prolonged the clotting time within 30 minutes to 3 to 4 times the control value and maintained antithrombotic levels for 6 to 8 hours in 75 per cent of the patients. The authors stated that the results indicate that this drug is a rapidly effective anticoagulant with prolonged action and without the rebound phenomenon of heparin. They suggested that it offers promise of gaining a place with heparin as an effective rapid anticoagulant.

The Effect of Vitamin B_{12} on Nitrogen and Phosphorus Metabolism in Patients With Pernicious Anemia. James, G. W., III and Abbott, L. D., Jr. Eastern Sect. Meet., Am. Fed. Clin. Res., Dec. 1950, through *Am. J. Med. 11*:516 (1951). The response in hemoglobin synthesis brought about by crystalline vitamin B_{12} in patients with pernicious anemia inspired further studies as an attempt to reveal the metabolic effects of this vitamin, particularly with regard to nitrogen and phosphorus metabolism. Four previously untreated patients with pernicious anemia were placed on a constant diet and observed for several weeks. The administration of the vitamin produced a prompt positive nitrogen balance as great as 6 Gm. per day. The hemoglobin produced amounted to 18 to 37 Gm. per day per patient for an average of 11 days. During this period the total nitrogen retained from diet sources equalled or was below the amount required for hemoglobin formation.

The authors reported that the following sequence of biochemical changes were observed in their studies: (1) a prompt and striking decrease in urinary phosphorus levels prior to any change in the reticulocyte count; (2) an increase in uric acid excretion during the rise in the reticulocyte count; and (3) and increase in phosphorus excretion during the period of greatest reticulocytosis. The authors, therefore, concluded from these clinical observations that the first metabolic effect of vitamin B_{12} seems to be a pronounced influence on nucleoprotein synthesis.

The Choice of Fluoridating Agents in the Control of Dental Caries. Howell, C. L., Burney, L. E., Day, H. G., and Muhler, J. C. *Am. J. Pub. Health* 42:44 (1952). Two methods of applying fluorides in the control of dental caries have been demonstrated as effective, namely, applying concentrated fluoride solutions topically to erupted teeth, and adjusting the fluoride content of the public water supply by the addition of a suitable fluorine compound. It has been shown that the application of a 2 per cent solution of sodium fluoride to the teeth of children from 7 to 17 years of age will reduce the incidence of caries by as much as 40 per cent. By adjustment of the communal water supply to a fluorine content of 1-1.2 p.p.m. with sodium fluoride it is possible to reduce the incidence of caries in the same age group of children by as much as 60 to 65 per cent, similar to the reduction observed using naturally occurring fluoridated water.

However, the authors pointed out that the choice of the fluoridating agent for use in communal water supplies should depend upon the verified ability of the agent to reduce caries, and not on the basis of cost, ease of handling, and engineering conveniences. A number of compounds are being tried, such as, sodium fluosilicate, hydrofluoric acid, hydrofluosilicic acid, calcium fluoride, tin fluoride, and sodium monofluorophosphate. However, there is insufficient evidence at the present time to justify the use of any fluorine compound other than sodium fluoride, except on an experimental basis, as the fluoridating agent of a communal water supply. The authors also pointed out that there is evidence that criteria other than the amount of fluorine available by chemical analysis must be considered when evaluating fluorine compounds intended for use as fluoridating agents in communal water supplies.

BOOK REVIEWS

The United States Public Health Service 1798-1950. By Ralph Chester Williams, 890 pages. Commissioned Officers Assoc. of U.S.P.H.S., 1951, Bethesda, Md.

The heritage of the Public Health Service of today goes back to very nearly the beginning of our national history. This book is a general presentation of the origin, organization and activities of the United States Public Health Service since its establishment in 1798. Factual emphasis has been placed on the progress and achievement of the commissioned corps of the U. S. P. H. S. in public health problems during the past half-century.

In addition to twelve chapters, which are very well indexed, a section on the source of material for the book has been included. No effort has been made to authenticate and support statements made by references to the literature. The growth of the Public Health Service and its tremendous impact on the development of Public Health is traced step by step, in the sequence of chapters.

Origin And Background (Hospitals); Quarantine (Guard Against Disease From Without); Promotions of Sanitation And Preventive Medicine (Evolution of Public Health); Scientific Understanding of Etiology And Treatment (Laboratory Research), Field Studies and Demonstrations (Epidemiology); Intragovernmental Relationships; (Coordination of Medical Activities); International Health Relations, (Consultation and Cooperation); Leadership and Leaders (Administration); Foundation of Public Health As A Career; Wartime Responsibilities; and the The Expanded Services of The Public Health Service Brought About by National and International Health Problems Today.

Reading this history should imbue everybody engaged in or interested in public health work with determination to carry forward the search for the application and betterment of knowledge for the improvement of Health.

BERNARD WITLIN

Pharmacopoea Internationalis, First Edition Volume I. World Health Organization, Geneva 1951. Columbia University Press, New York. Price $5.00.

The First Volume of the long anticipated International Pharmacopoeia, published under the auspices of the World Health Organization of the United Nations, was first released at the meeting of the International Pharmaceutical Federation, at Rome, in September, 1951. It is now available through all of the distributing agents of the United Nations throughout the world. In the United States, this agency is The Columbia University Press, New York City. It may be obtained in either English or French and a Spanish edition will soon be available.

This First Volume provides standards and Latin titles for 199 items; mostly, therapeutically active substances and pharmaceutic necessities with a few preparations of the basic drugs, and an appendix providing general test methods, doses, tables, etc.

A Second Volume has been completed and is being placed in type. This will be largely made up of preparations in forms best adapted for the efficient administration of the therapeutic agents in Volume I. Volume II will also include some basic drugs; especially, the antibiotics and other important medicinal agents of recent development for which standards were not available for Volume I.

An additional Volume, the Third, is also in preparation to furnish other important new standards now under review by the International Committee. In fact, the International Pharmacopoeia, as now planned, will maintain a continuous revision with the Committee meeting twice a year, usually in Geneva, and, in the interim, carrying out the revision studies in the various laboratories of the members in their respective countries. All circulars and communications are issued through the office of the permanent Secretary located at Geneva.

A comprehensive review of Volume I, issued by the Chairman of the International Committee, Dr. C. H. Hampshire, will be found in this issue of the Journal, pages 64-68.

E. Fullerton Cook

Check Your Stock!

Methajade®

ANTITUSSIVE

Contains Methadone HCl

FOR COUGH CONTROL

Prescriptions for delicious, lime-flavored METHAJADE® Antitussive will be heavy during the next few months. Check your stock *today* and reorder at once to prevent lost sales on this fast-moving ethical antitussive preparation.

Each fluidounce of emerald green METHAJADE contains methadone hydrochloride, 10 mg., and PROPADRINE® phenylpropanolamine hydrochloride, 0.12 Gm., with potassium citrate, 1.2 Gm., diluted phosphoric acid, 4.5 cc., and alcohol, 5%. Exceptionally effective control of cough reflex; also relaxes muscles of the bronchi. Supplied in pint *Spasaver*® and gallon bottles.

Note: Remind your physicians that methadone hydrochloride requires a narcotic prescription.

Sharp & Dohme, Philadelphia 1, Pa.

Cancer strikes one in five

Strike back

Your Dollars *will save li*
by strengthening the Can
Crusade of the Americ
Cancer Society.

Your Dollars *will bring wo*
of truth and hope to you,
your family, to your frie
and to your community.

Your Dollars *will help e*
the pain of the cancer pati

Your Dollars *will train sk*
ed, understanding hands
minds to serve in the hospi
in the doctor's office, perh
even in your home.

Your Dollars *will speed*
march of research tow
mastery over cancer, the
ease that last year ki
215,000 men, women and c
dren.

Give to conquer cancer

American Cancer Society

Mail the coupon to "Cancer"
C/O your local Post Office

AMERICAN CANCER SOCIET
GENTLEMEN:
☐ PLEASE SEND ME
LITERATURE ABOUT CANCER.
☐ ENCLOSED IS MY
TRIBUTION OF $.....TO
CANCER CRUSADE.

Name.....
Address.....
City.....State.....

American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

Former Editors of the Journal have been: Daniel B. Smith, 1825-1828; Benjamin Ellis, 1829-1831; Robert E. Griffith, 1831-1836; Joseph Carson, 1836-1850; William Procter, Jr., 1850-1871; John M. Maisch, 1871-1893; Henry Trimble, 1893-1898; Henry Kraemer, 1898-1917; George M. Beringer, 1917-1921, and Ivor Griffith, 1921-1941.

Established and maintained as a record of the progress of pharmacy and the allied sciences, the Journal's contents and policies are governed by an Editor and a Committee on Publications elected by the members of the College.

Manuscripts should be sent to the Editor, who does not assume any responsibility in connection with the views or investigations of contributors of accepted manuscripts, other than to exercise general care in selection.

Contributors are allowed a reasonable number of copies of this Journal, free of charge, if applied for when the proof is returned.

Reprints, if desired, should be ordered when the proof is returned. The table below shows the *approximate* cost of reprints, the make-up of the pages to be identically the same as in the Journal. The actual cost may vary from the figures given, and will depend upon the amount of presswork, paper, binding, and other factors. Reprints containing half-tones may be expected to cost somewhat more than the rates given.

	2 pp.	4 pp.	8 pp.	16 pp.
50 copies	$3.50	$6.00	$10.50	$11.25
100 "	4.25	7.00	14.00	15.00
250 "	5.25	9.00	18.75	20.00

Covers with Titles	
50 copies	$ 5.00
100 "	6.50
250 "	10.25


Give!